UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

DK

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/315,298	05/20/99	TENG C	ISIS-3510

HM22/0923

MICHAEL P STRAHER
WOODCOCK WASHBURN KURTZ MACKIEWICZ
& NORRIS LLP
ONE LIBERTY PLACE 46TH FLOOR
PHILADELPHIA PA 19103

EXAMINER
EPPS, J

ART UNIT	PAPER NUMBER
1635	5

DATE MAILED: 09/23/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/315,298	Applicant(s) Teng et al.
	Examiner Janet Epps	Group Art Unit 1635

☒ Responsive to communication(s) filed on *May 20, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-83* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-83* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Objections

1. Claims 81-83 are objected to because of the following informalities: Claims 81-83 refer to oligonucleotides having a defined nucleotide sequence, such sequence disclosures should be referred to by the appropriate sequence identifier (SEQ ID NO:#) which corresponds to the sequence listing for this application. Appropriate correction is required.

Double Patenting

2. Claims 1-75 of this application conflict with claims 1-75 of Application No. 09/082,624. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claims 1-75 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-75 of copending Application No. 09/082,624. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 3 and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3 and 54 are drawn to oligonucleotides which "modulates the expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses". According to these claims all oligonucleotides which modulate the expression of "a cellular adhesion protein...a rate of cellular proliferation.." are contained within the broadest reasonable interpretation of these claims. However, the specification describes only oligonucleotides included in Tables 1-6 of the specification. Tables 1-6 do not include every conceivable oligonucleotide which "modulates the expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses". Since the design of oligonucleotides particularly antisense

molecules and ribozymes requires the knowledge of the target sequence, the structure of oligonucleotides (e.g. antisense and ribozymes) which "modulates the expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses" from all possible sources can not be determined without knowledge of all the sequences of genes which function as cellular adhesion proteins, in cellular proliferation, or the sequences of the genomes of all possible eukaryotic pathogens or retroviruses. The specification as filed does not describe all the possible antisense structures that are encompassed by the claimed genus, but only provides prophetic teachings that antisense oligonucleotides could be made. The specification clearly fails to describe a representative number of species to allow one skilled in the art to envisage the structures of all members of the claimed genus.

Therefore, applicants are not in possession of all oligonucleotide(s) which " modulates the expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses" from any other source except those disclosed within the specification of the instant application.

7. Claims 1-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of expression of a cellular adhesion protein, inhibition of a rate of cellular proliferation, inhibition of the biological activity of eukaryotic pathogens or retroviruses *in vitro*, does not reasonably provide enablement for inhibition of of a cellular adhesion protein, inhibition of a rate of cellular proliferation, inhibition of the biological activity of

eukaryotic pathogens or retroviruses *in vivo*, nor does it provide enablement for "modulation" (which includes both inhibition and enhancement) of expression of a cellular adhesion protein, ~~inhibition~~ of a rate of cellular proliferation, ~~inhibition~~ or of the biological activity of eukaryotic pathogens or retroviruses , *in vitro* or *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

A.C.E. 9/22/99

These claims are drawn to compositions comprising an oligonucleotide in some type of carrier and methods of administering these oligonucleotides which "modulates the expression of a cellular adhesion protein, modulates of a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses", for purposes of treatment of conditions related to the activity of eukaryotic pathogens, retroviruses, cellular adhesion proteins or cellular proliferation. According to the specification, the term oligonucleotide refers to antisense, ribozymes, a peptide nucleic acid, a molecular decoy, an external guide sequence or an aptamer. If the scope of the claims are truly limited to antisense based molecules only inhibition is enabled not modulation, since modulation implies increasing and decreasing expression. The specification does not teach increasing the expression of a cellular adhesion protein, a rate of cellular proliferation, or increasing the biological activity of eukaryotic pathogens or retroviruses. The state of the art for antisense based systems does not teach increase in expression or biological activity, except in rare instances. Since this specification does not teach increase in expression or biological activity

and since the state of the art of antisense based systems teach only inhibition, applicants claim to "modulate" is not enabled to the extent that it reads on an antisense based system.

8. The pharmaceutical composition and methods of use referred to in claims 1-83 implies *in vivo* applicability for enablement purposes. There are no general guidelines for successful *in vivo* delivery of antisense/ribozyme compounds currently known in the art, nor are such guidelines provided in the specification as filed. Crooke (1998), states that "extrapolations from in vitro uptake studies to predictions about *in vivo* pharmacokinetic behavior are entirely inappropriate". According to Branch (1998), the successful delivery of antisense/ribozymes *in vivo* is unpredictable, the internal structures of the targeted RNAs and their association with cellular proteins can render target sites totally unaccessible *in vivo*. In addition, Branch also notes that effective nucleic acid drugs are currently selected from large pools of candidates, suggesting that the amount of experimentation in the art is significant. See Gura which states: "The uncertainty about what antisense drugs are doing inside the body has caused some experts in the field to argue that clinical trials have begun far too soon". Stanley Crooke says, in Antisense '97, "Never in the history of drug discovery and development has anyone attempted to correlate the pharmacokinetics with any class of drugs with cellular uptake *in vitro*". Therefore, the specification does not describe the use of oligonucleotides (antisense based) which inhibit the expression of a cellular adhesion protein, a rate of cellular proliferation, or inhibition of a eukaryotic pathogen or retrovirus of these claims in a sufficient manner so as to enable one of

ordinary skill in the art to practice the present invention without undue experimentation. These conclusions are based upon the known unpredictability regarding the delivery of antisense *in vivo* and further with secondary effects such as treating conditions related to the expression of a cellular adhesion protein, cellular proliferation, the activity of a eukaryotic pathogen or a retrovirus in a patient, and the lack of guidance in the specification as filed in this regard.

The quantity of experimentation required to practice the invention as claimed would require determining modes of delivery in a whole organism such that the desired nucleic acid molecule is targeted and its expression and/or biological activity is inhibited and the desired secondary effects (treatment leading to the amelioration of conditions associated with expression of a cellular adhesion protein, cellular proliferation, the activity of a eukaryotic pathogen or a retrovirus in a patient) are obtained. The specification as filed provides no specific guidelines in this regard. The deficiencies in the specification would constitute undue experimentation since these steps must be achieved without instructions from the specification before one is enabled to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps whose telephone number is (703) 308-8883. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached at (703) 308-4003. The fax number for this group is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

George C. Elliott, Ph.D.
Supervisory Patent Examiner
Technology Center 1600

Janet L. Epps, Ph.D.

September 21, 1999